REMARKS

Claims 1-4 are pending in the instant application. Claims 1-4 have been rejected. Claims 1, 2 and 4 have been amended. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. **Rejection of Claims Under 35 U.S.C. §112**

Claims 1-4 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not disclosed in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner suggests that there is no support in the specification for a method for identifying compounds comprising determining a first level of transcription detected in cells containing interacting proteins comprising a Smad protein and a Smad protein co-repressor. In particular, it is suggested that there is not support for the claimed method to include a *Smad protein* co-repressor in the assay comprising interacting proteins. Applicant respectfully traverses this rejection.

Applicant respectfully disagrees with the Examiner's suggestion that the instant application provides no support for the claimed method including a Smad protein co-repressor. MPEP 2106 indicates that the "claimed subject matter need not be described literally, *i.e.*, using the same terms, in order for the disclosure to satisfy the description requirement." At page 14, lines 11-21, the specification states that "assays can be developed, for example to identify proteins or small molecules that interact with Smad proteins to prevent interactions of CtBP

with Smads or with *DNA-binding co-repressors* (*e.g.*, Evi-1, TGIF, SIP1 or *Schnurri*), or formation of a *DNA-bound complex containing Smad, CtBP and DNA binding co-repressors...*" and Schnurri is described as a "*DNA*-binding *Smad co-repressor*" at page 7, lines 17-18. Therefore, while not literally stating that Evi-1, TGIF and SIP1 are *DNA-binding Smad co-repressors*, because these proteins are functionally equivalent to Schnurri, these proteins would likewise be considered *DNA-binding Smad co-repressors*. To advance the prosecution of the present application, Applicant has further amended claims 1 and 2 to indicate that the Smad co-repressor is a "DNA-binding Smad co-repressor".

Applicant further respectfully disagrees with the Examiner's suggestion that the specification does not support the contemplation of a complex of interacting proteins comprising a Smad protein, a DNA-binding Smad co-repressor protein and a CtBP protein as the specification at page 7, lines 17-18, specifically states that these proteins form a DNA-bound complex which inherently indicates that they interact. Withdrawal of this rejection is therefore respectfully requested.

Claims 1-4 further stand rejected under 35 U.S.C. §112, second paragraph, as being vague and indefinite in the method steps. The Examiner suggests that it is not clear what genes or genes are being transcribed or what molecule's transcription level should be detected. It is further suggested that it is not clear from the method steps how the level of transcription is determined or detected and how a comparison of levels of transcription is implemented. The Examiner acknowledges that while the methods steps need not contain every technical detail, that they should at least include reagents necessary for the

assay, a detection step in which the reaction products are quantitated or visualized and a correlation step describing how the results of the assay allows the determination of compounds that directly interact with a Smad or a Smad protein co-repressor.

In an effort to advance the prosecution of the instant application, Applicant has indicated the necessary reagents for the assay (*i.e.*, a reporter with a Smad box-containing promoter in cells containing interacting proteins comprising a Smad protein, a DNA-binding Smad co-repressor protein and a CtBP protein); steps for detecting a first and second level of transcription of the reporter in the cells before and after addition of the test compound, respectively; and a correlation step which compares the first level with the second level, wherein a decrease in the level of repression of transcription of the reporter in said cells after addition of the test compound is indicative of the ability of the test compound to interfere with transcriptional repression of genes induced by a TGF-β, activin or bone morphogenetic protein signal in cells. Support for these amendments can be found upon reading the disclosure in whole and in particular at the paragraph bridging pages 14 and 15 which discloses the use of a cell-based reporter assay for use in screening for compounds that disrupt repression by TGF-β and page 9 and Figure 3 which teach the use of a Smad box-LacZ reporter assay for detecting the effect of dCtBP on activation of gene expression by Mad, Medea, and tkv. Withdrawal of this rejection is therefore respectfully requested.

Claim 4 is also rejected under 35 U.S.C. §112, second paragraph, as being vague and indefinite in the recitation of "a

homologue of dCtBP." The Examiner suggests that it is not clear what type of molecule is deemed an analogue of dCtBP as it is not clear if the homologue is a duplicate, structurally equivalent and/or functionally equivalent to the wild-type dCtBP.

Applicant has therefore amended claim 4 to clarify that a homologue of dCtBP is a functional homologue as indicated at page 8, lines 22-25, which teaches that dCtBP and its homologs function as co-repressors and have the ability to bind histone deacetylase. Such functional homologs were well-known at the time of filing. See reply to Office Action mailed September 8, 2003. Withdrawal of this rejection is therefore respectfully requested.

II. Conclusion

The Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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